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Updates to DISC, TRAN, CLIN Concepts

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CIRM
CALIFORNIA'S STEM CELL AGENCY

Main Changes to DISC2 Concept

1. **Award duration:**
   - **Therapeutic Candidate (TC) Awards**: Change **maximum duration** from **2** years **to 3** years
2. **Budget:**
   - **TC: Baseline increased** from **$900K** to $**1.5M** direct costs:
     - **Scaled baseline** from 24 months to 36 months
     - **Accounted for an overall *increase in project costs* from 2017-2022** (*)
   - **Up to** an additional $200K *may be requested* with **strong** justification for:
     - Activities related to obtaining and/or sharing development compatible lines (**), testing multiple lines to ensure quality of selected DC, and addressing scientific diversity.

(*) Weighted average between: Predoc/Post doc stipends up by ~20% since 2017 (CIRM) / Personnel salary cap raised by 15% since 2017 (CIRM) / Cost of goods/general inflation up 14% since 2017 (US gov data)
(**) CIRM will be requiring development compatible PSC lines for relevant DC awards, and where appropriate, encouraging the inclusion of multiple lines to improve rigor and address diversity.

Main Changes to DISC2 and TRAN Concept

- Allow **90 days to launch awards:** originally PA allowed 120 days, reduced to 30 days in 2020 for urgent programs. Changed to 60 days in 2021 but remains challenging now that more awards are being made per cycle. 90 days is a more comfortable window that allows project teams to hire/place key personnel.

Main Changes to CLIN2 Concept

Basis for award maximum and co-funding amounts

Clinical trial studies where testing of a therapeutic candidate in a given disease indication and using a given route of administration are:

- First in-human studies
  - Award Max: $12M (non-profit), $8M (for-profit)
  - Co-funding: None (non-profit), 30% (for-profit)
- Succeeding studies
  - Award Max: $15M non-profit and for-profit
  - Co-funding: 40% non-profit and for-profit

Main Changes to CLIN1 Concept

Addition of Allogeneic Donor Cell Eligibility from DISC/TRAN Concepts

- For all projects developing a product candidate that includes allogeneic (donor-derived) cells:
  - The cell source (tissue or cell line) proposed for use must have been consented by the donor for intended use and for clinical development and commercial sale
  - The cells must meet the Good Tissue Practices (GTP) requirements for donor eligibility (21 CFR 1271 (subpart C)), or there is plan in place to address the GTP requirements

Global Changes to DISC, TRAN, and CLIN Concepts

- Data Sharing Plan requirements
  - Make data sharing itself a requirement in addition to the currently required sharing plan
- Updated DEI language
  - Updating to reflect consolidation of DEI sections & Board feedback
- Removing expired references to CIRM 2.0, streamlining format
  - Creating easier to read templates that present key information clearer

Global Changes to DISC, TRAN and CLIN Concepts

- Consistency of eligible candidates across concepts
  - For example, allow min manipulated bone marrow, cord, unmodified HSC in TRAN, which is allowed in DISC and CLIN
  - Question: Do we align DISC0 genetic research definition with gene therapy definition (i.e., expand candidates eligible as gene therapy)?

Gene Therapy vs Genetic Therapy

Current Gene Therapy Scope

CIRM considers gene therapy to mean a human therapeutic intervention intended to:

1) alter the genomic sequence of cells or
2) alter the cellular lineage or function via gene delivery (i.e., direct lineage reprogramming).

The intervention may include strategies to repair a disease-causing gene sequence, remove or inactivate a disease-causing gene, or introduce new or modified genes that augment the therapeutic potential of the target cells.

Gene therapy approach must be intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs.

Definition initially approved by ICOC prior to Proposition 14

Proposed Genetic Therapy Scope

CIRM considers genetic therapy to mean research that:

1) alters genomic sequences of cells (edit, remove, or add DNA sequences)

or

2) introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells.

Genetic therapy approach must be intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs.

Proposition14 allows funding of “genetic research”